REMARKS

In the present amendment, Applicant has amended the claims to recite "administering intratracheally or intrabronchially" and to recite the PDE5 inhibitor "SILDENAFIL or a pharmaceutically acceptable salt thereof". Applicant has also amended claim 3 to remove recitation of "preventing" and replace it with "treating". Support for these amendments are found in the orginal specification, for example, at page 12, third paragraph; page 14, second paragraph; and page 18, second paragraph. Also, Applicant cancels claims 6, 13, 16-25, 29-33, and 36-48 withdrawn from consideration as being drawn to non-elected subject matter, and claims 9-12, 14, and 34-35, without prejudice or disclaimer to the subject matter recited therein. The amendments do not introduce new matter within the meaning of 35 U.S.C. § 132. Claims 3-5, 7, 8, and 15 are pending and remain under examination.

1. Objections to the Claims

The Office objects to claim 14 as depending from a non-elected claim, and objects to claim 10 as being a substantial duplicate of claim 9. These objections are rendered moot in view of the above amendment canceling claims 9, 10, and 14. Accordingly, Applicant respectfully requests entry of the amendment and withdrawal of the objections.

2. Rejection of Claims 1-17 under 35 U.S.C. §112, 1st paragraph

The Official Action states that claims 3-5, 7-12, 14-15, and 34-35 are rejected under 35 U.S.C. §112, 1st paragraph, for failing to comply with the enablement requirement. The

Office asserts that the specification, while being enabling for methods to evaluate the treatment by pulmonary surfactants and PDE5 inhibitors individually, does not reasonably provide enablement for the prevention of diseases that originate from pulmonary surfactant malfunction and detrimental PDE5 activity by the synergistic administration of pulmonary surfactants and PDE5 inhibitors. Applicant traverses the rejection

However, in order to advance prosecution, and without acquiescence or disclaimer, Applicant has amended claim 3 to remove the recitation of "preventing" and replaced it with the recitation of "treating".

Applicant submits that one of skill in the art reading the specification would understand that the specification includes both adequate written description and enablement for a method for treating the onset of symptoms of a disease in which pulmonary surfactant malfunction and/or phosphodiesterase 5 (PDE5) activity is detrimental. For example, the specification at page 18, second paragraph, provides detailed written description of treating the onset of symptoms of a disease in which pulmonary surfactant malfunction and/or phosphodiesterase 5 (PDE5) activity is detrimental. Additional evidence that the specification enables the claims is also shown in the supplemental experimental data presented in the expert's declaration filed herewith. The declaration provides additional evidence of the superadditive therapeutic effect of intratracheal and intrabracheal administration of pulmonary surfactant with Sildenafil as described in the specification.

Accordingly, the specification enables the claims. Applicant respectfully requests that the Examiner reconsider and withdraw this rejection.

3. Rejection of Claims 3, 9-12, 15, 34-35 Under 35 U.S.C. §102

Claims 3, 9-12, 15, 34-35 are rejected as anticipated under 35 U.S.C. § 102 over Wilkins et al., Clinical Techniques in Equine Practice 2:56-66 (2003) ("Wilkins"). As a basis for this rejection, the Office alleges that Wilkins discloses intravenous administration of Sildenafil (page 59, first column, first paragraph), and discloses treatment of surfactant dysfunction, by instilling exogenous surfactants (page 65, first column, second paragraph.)

Applicant traverses the rejection because the claims recite administering the compositions intratracheally or intrabronchially, which are distinguished from the intravenous administration of Sildenafil disclosed in Wilkins.

Furthermore, even if the claims did not recite mode of administration, Wilkins would still not anticipate the claims because Wilkins does not teach the recited administration of both surfactant and Sildenafil to an individual patient.

Accordingly, Wilkins does not anticipate the claims. Applicant respectfully requests that the Examiner reconsider and withdraw this rejection.

4. Rejection of Claims 3-5, 7-12, 15, and 34-35 Under 35 U.S.C. §103

Claims 3-5, 7-12, 15, and 34-35 are rejected as obvious under 35 U.S.C. § 103 over Wilkins in view of WO 01/76619 to Hafner et al. ("Hafner"). As a basis for this rejection, the Office alleges that Wilkins discloses intravenous administration of Sildenafil, a known PDE5 inhibitor, as an investigational pulmonary therapy (page 59, first column, first paragraph), and further discloses treatment of surfactant dysfunction, by instilling

exogenous surfactants (page 65, first column, second paragraph.) The Office admits that Wilkins does not teach the co-administration of the pulmonary surfactant and Sildenafil. The Office applies Hafner as teaching use of pulmonary surfactant protein lusupultide for the treatment of pulmonary diseases (claim 6). The Office admits that Hafner does not teach the use of administering a PDE5 inhibitor.

The Office then relies upon *In re Kerkhoven*, and appears to assert that it is obvious that "the combination of two or more compositions each of which is taught by the prior art to be useful for the same purpose in order to form a third composition which is to be used for the very same purpose." The Office thus asserts it would have been obvious to combine the administration of Sildenafil and lusupultide. One would have been motivated to co-administer them in view of the teachings of Wilkins and Hafner which individually teach the use of Sildenafil and lusupultide for the treatment of pulmonary diseases.

RESPONSE

Applicant respectfully traverses the rejection of claims 3-5, 7-12, 15, and 34-35. One of ordinary skill in the art would not have been motivated to combine the disclosures of Wilkins and Hafner to devise the Applicant's inventive subject matter as a whole as recited in the claims. Thus, the Examiner has failed to establish a *prima facie* case of obviousness against the presently rejected claims.

To establish a *prima facie* case of obviousness, the PTO must satisfy three requirements. First, the prior art relied upon, coupled with the knowledge generally available in the art at the time of the invention, must contain some suggestion or incentive

that would have motivated the skilled artisan to modify a reference. *In re Fine*, 5 USPQ2d 1596, 1598 (Fed. Cir. 1988). Second, the proposed modification of the prior art must have had a reasonable expectation of success, determined from the vantage point of the skilled artisan at the time the invention was made. *Amgen Inc. v. Chugai Pharm. Co.*, 18 USPQ2d 1016, 1023 (Fed. Cir. 1991). Lastly, the prior art references must teach or suggest all the limitations of the claims. *In re Wilson*, 165 USPQ 494, 496 (C.C.P.A. 1970).

A. No *prima facie* case of obviousness has been shown by the Examiner

The Examiner has failed to show a *prima facie* case of obviousness because there is no motivation to combine the teachings of the cited references.

Although Wilkins and teaches the use of one or more of dozens of different anti-inflammatory agents in a kappa opioid composition, the references in combination with the knowledge of one of ordinary skill in the art does not provide a specific example where a pulmonary surfactant and PDE5 inhibitor are co-administered to form a specific composition of the present claims.

Applicant submits that *In re Kerkhoven* has been improperly relied upon by the Office, and does not support the Office's rejection. The facts and holding of *In re Kerkhoven* involved "combin[ing] two compositions each of which is taught by the prior art to be useful for the same purpose." *In re Kerkhoven*, 205 USPQ 1069, 1072 (CCPA 1980) (emphasis added). However, in contrast to *Kerkhoven,* in the present case the Examiner does not appear to be combining pulmonary treatment compositions. Rather, in an effort to reproduce Applicant's claimed invention, the Examiner is picking and choosing individual

components from the isolated disclosures of Wilkins and Hafner of one or more numerous pulmonary treatment agents that can be used in combination with the claimed method. However, "[s]uch piecemeal reconstruction of the prior art patents in light of [Applicant's] disclosure is contrary to the requirements of 35 U.S.C. 103." *In re Wesslan*, 147 USPQ 391, 393 (CCPA 1965). If the Office did actually suggest the combination of pulmonary treatment compositions themselves this point has not been made clear on the record.

Therefore, a prima facie case of obviousness has not been shown, and Applicant respectfully requests that the Office reconsider and withdraw the rejections.

B. Superadditive Effect rebuts a *prima facie* case of obviousness

If, however, the Office insists on maintaining that the presently pending claims are obvious in view of the deficient teachings of the cited references, Applicant respectfully draws the Examiner's attention to Figure 1 of the attached declaration under 37 CFR 1.132 which unexpectedly demonstrates a much higher reoxygenation due to intratracheal (i.t.) administration of a pulmonary surfactant in combination with Sildenafil in the rat lung lavage model of reoxygenation. Neither the prior art nor one of skill in the art would have expected such a superadditive effect of combined administration of Sildenafil and a pulmonary surfactant. Thus, the data submitted herewith in the 1.132 declaration unexpectedly shows that the presently claimed method for treating or reducing the onset of symptoms of a disease in which pulmonary surfactant malfunction and/or phosphodiesterase 5 (PDE5) activity is detrimental, or treating or reducing the severity of a

disease in which pulmonary surfactant malfunction and/or phosphodiesterase 5 (PDE5) activity is detrimental in a patient, comprising administering intratracheally or intrabronchially to a patient in need thereof an effective amount of (1) a pulmonary surfactant and (2) SILDENAFIL or a pharmaceutically acceptable salt thereof results in a superadditive effect of combined administration of Sildenafil with a pulmonary surfactant.

These results are unexpected in view of the teachings of the prior art which merely shows that a pulmonary surfactant and Sildenafil can each be used separately to treat various pulmonary disorders using different routes of administration than those presently claimed. As such, a person of ordinary skill in the art would not expect that combining these two different treatments in a different route of administration would provide synergistic effects in treating a disease by treating or reducing the onset of symptoms of a disease in which pulmonary surfactant malfunction and/or phosphodiesterase 5 (PDE5) activity is detrimental, or treating or reducing the severity of a disease in which pulmonary surfactant malfunction and/or phosphodiesterase 5 (PDE5) activity is detrimental in a patient. Accordingly, the Examiner is respectfully requested to reconsider and withdraw the rejection of claims 3-5, 7-12, 15, and 34-35 under 35 USC §103(a).

Applicants note that the declaration under 37 CFR 1.132 filed herewith also provides experimental data for specific, presently unclaimed, combinations of PDE5 inhibitors and pulmonary surfactants which do not exhibit superadditive effects when co-administered in the rat lung lavage model of reoxygenation. (For example, see Figures 2, 3, and 4.)

CONCLUSION

Based upon the above remarks, the presently claimed subject matter is in condition for allowance. The Examiner is therefore respectfully requested to reconsider and withdraw the present objection to the claims, as well as the rejection of all pending claims 3-5, 7, 8, and 15. Favorable action with an early allowance of the claims pending in this application is earnestly solicited.

The Examiner is welcomed to telephone the undersigned attorney with any questions or comments.

Respectfully submitted,
NATH LAW GROUP, PLLC

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Attachment:
Declaration Under 37 CFR 1.132